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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,930	10/03/2005	Kevin Liu	K0002-502-US	1998
51625	7590	08/18/2008	EXAMINER	
GLOBAL PATENT GROUP - KAL			WILLIS, DOUGLAS M	
ATTN: MS LAVERN HALL			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/551,930	Applicant(s) LIU ET AL.
	Examiner DOUGLAS M. WILLIS	Art Unit 4161

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 01 August 2008.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 123-126,130-133 and 143-145 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 123-126,130-133, 143 and 145 is/are rejected.

7) Claim(s) 144 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date 04-16-07.

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.

5) Notice of Informal Patent Application

6) Other: _____.

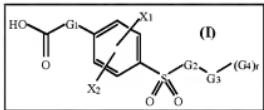
DETAILED ACTION

Status of the Claims / Priority

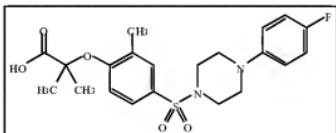
Claims 123-126, 130-133 and 143-145 are pending in the current application. According to the *Amendments to the Claims*, filed August 1, 2008, claims were renumbered to start with 123 and proceed to 145 to correct a numerical error. Furthermore, according to this same *Amendment*, claims 123-125 and 130-133 were amended, claims 127-129 and 134-142 were cancelled and claims 143-145 were added. This application is a 35 U.S.C. § 371 National Stage Filing of International Application No. PCT/US2004/10889, filed April 7, 2004, which claims priority under 35 U.S.C. § 119(a-d) to US Provisional Application No. 60/461,577, filed April 7, 2003.

Restrictions / Election of Species

Applicant's provisional election of the following, with traverse, in the reply filed on



August 1, 2008, is acknowledged: a) Group I, claims 123-145; and b) compound of Formula (I) - example 39, p. 63, shown right below, wherein $G_1 = -C(R^1R^2)_nO-$, wherein $R^1 = -CH_3$ (C_{1-4} alkyl), $R^2 = -CH_3$ (C_{1-4} alkyl) and $n = 1$; $G_2 =$ -piperazine; $G_3 =$ -a single bond; and $G_4 = -Ph$ (aryl), optionally substituted with -F, where $r = 1$, and hereafter referred to as 2-(4-(4-(4-fluorophenyl)piperazin-1-ylsulfonyl)-2-methylphenoxy)-2-methylpropanoic acid.



Affirmation of this election must be made by applicant in replying to this Office action.

The traversal is on the ground(s) that the examiner's restriction, as laid out between Groups I and II, is directed, in part, to subject matter contained within individual Markush claims and thus is not permitted by 35 U.S.C. § 121. This is not found persuasive because the multiple compounds recited by the Markush structure in the instant application are independent and/or distinct for the reasons disclosed in the *Requirement for Restriction / Election of Species*, mailed on June 25, 2008. Furthermore, there would be a serious burden on the examiner if restriction was not required because the inventions have acquired a separate status in the art due to their divergent subject matter and would require a different field of search.

The requirement is still deemed proper and is therefore made FINAL.

The elected species, shown above, was found to be free of the prior art. Thus, the examiner has expanded the forthcoming prosecution to include all claims relevant to the genus of Group I, for a first Office action and prosecution on the merits.

Claims 127-129 and 134-142 would have been withdrawn from further consideration, pursuant to 37 CFR 1.142(b), but were previously cancelled via *Amendment* by applicant, as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Thus, a first Office action on the merits of claims 123-126, 130-133 and 143-145 is contained within.

Claim Objections

Claim 123 is objected to because of the following informalities: the term *cycloheteroaryl* lacks meaning in the chemical art and no definition is provided in the Specification for this term. The examiner asserts that for a compound to be *aromatic* it would indeed need to be cyclic and fully conjugated; however, the term *cycloheteroaryl* may not be limited to this scope, since both

aryl and heteroaryl are appropriately defined in the Specification. Appropriate corrective action is required.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

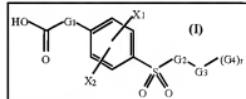
Claims 123-126, 130-133, 143 and 145 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein $R^1 = -H$ or $-C_{1-4}\text{alkyl}$; $R^2 = -H$ or $-C_{1-4}\text{alkyl}$; $X_1 = -H$ or $-C_{1-4}\text{alkyl}$; $X_2 = -H$ or $-C_{1-4}\text{alkyl}$; $X_3 = -H$ or $-C_{1-4}\text{alkyl}$; $X_4 = -H$ or $-C_{1-4}\text{alkyl}$; and $G_4 = -\text{aryl}$, $-\text{heteroaryl}$ or $-\text{cycloalkyl}$, does not reasonably provide enablement for substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein $R^1 = -C_{1-4}\text{heteroaryl}$, $-C_{1-4}\text{alkoxy}$ or $-C_{1-4}\text{perhaloalkyl}$; $R^2 = -C_{1-4}\text{heteroaryl}$, $-C_{1-4}\text{alkoxy}$ or $-C_{1-4}\text{perhaloalkyl}$; $X_1 = -\text{cycloalkyl}$, $-\text{halogen}$, $-\text{perhaloalkyl}$, $-\text{hydroxy}$, $-\text{nitro}$, $-\text{cyano}$, $-C_{1-4}\text{alkoxy}$ or $-\text{NH}_2$; $X_2 = -\text{cycloalkyl}$, $-\text{halogen}$, $-\text{perhaloalkyl}$, $-\text{hydroxy}$, $-\text{nitro}$, $-\text{cyano}$, $-C_{1-4}\text{alkoxy}$ or $-\text{NH}_2$; $X_3 = -\text{halogen}$, $-C_{1-4}\text{perhaloalkyl}$, $-\text{hydroxy}$, $-\text{alkoxy}$, $-\text{nitro}$, $-\text{cyano}$ or $-\text{NH}_2$; $X_4 = -\text{halogen}$, $-C_{1-4}\text{perhaloalkyl}$, $-\text{hydroxy}$, $-\text{alkoxy}$, $-\text{nitro}$, $-\text{cyano}$ or $-\text{NH}_2$; and $G_4 = -\text{cycloalkenyl}$ (hereafter collectively referred to as *condition A*), or pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention(s) commensurate in scope with these claims. Substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, or

pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates thereof, as recited in claim 123, have not been adequately enabled in the specification to allow any person having ordinary skill in the art, at the time this invention was made, to make and use substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, or pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates thereof.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is *undue*. These factors include, but are not limited to: (a) breadth of the claims; (b) nature of the invention; (c) state of the prior art; (d) level of one of ordinary skill in the art; (e) level of predictability in the art; (f) amount of direction provided by the inventor; (g) existence of working examples; and (h) quantity of experimentation needed to make or use the invention based on the content of the disclosure. (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The above factors, regarding the present invention, are summarized as follows:

- (a) *Breadth of the claims* - the breadth of the claims includes all of the tens of thousands of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), shown right, as well as the myriad of potential *N*-oxides, prodrugs, metabolites, amides or solvates, formulated from these substituted benzene sulfonamides and pharmaceutical compositions of the formula (I);
- (b) *Nature of the invention* - the nature of the invention is evaluation of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I) and the pharmacokinetic behavior of these substances in the human body as modulators of peroxisome proliferator activated receptors (PPARs);
- (c) *State of the prior art* - *Nature Reviews: Drug Discovery* offers a snapshot of the state



of the drug development art. Herein, drug development is stated to follow the widely accepted Ehrlich model which includes: 1) development of a broad synthetic organic chemistry program; 2) subsequent testing of compounds in an appropriate laboratory model for the disease to be treated; and 3) screening of compounds with low toxicity in prospective clinical trials (Jordan, V. C. *Nature Reviews: Drug Discovery*, 2, 2003, p. 205);

- (d) *Level of one of ordinary skill in the art* - the artisans synthesizing applicant's substituted benzene sulfonamides and pharmaceutical compositions of the formula (I) would be a collaborative team of synthetic chemists and/or health practitioners, possessing commensurate degree level and/or skill in the art, as well as several years of professional experience;
- (e) *Level of predictability in the art* - Synthetic organic chemistry is quite unpredictable (*In re Marzocchi and Horton* 169 USPQ at 367 ¶ 3). The following excerpt is taken from Dörwald, which has extreme relevance to the synthesis of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, and pharmaceutically acceptable *N*-oxides, metabolites or amides thereof (Dörwald, F. Zaragoza. *Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design*, Weinheim: WILEY-VCH Verlag GmbH & Co. KGaA, 2005, Preface):

Most non-chemists would probably be horrified if they were to learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why.

Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work.

Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious).

Similarly, the following excerpt is taken from Vippagunta, et al. with respect to pharmaceutically acceptable solvates of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant

(Vippagunta, et al. *Advanced Drug Delivery Reviews*, 48, 2001, p. 18):

Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates

Finally, the following excerpt is taken from Burger's with respect to the synthesis of prodrugs of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein condition A is relevant (Wolff, Manfred E., Ed. *Burger's Medicinal Chemistry and Drug Discovery - Fifth Edition*, New York: John Wiley & Sons, 1996, vol. 1, pp. 975-976):

The design of prodrugs in a rational manner requires that the underlying causes which necessitate or stimulate the use of the prodrug approach be defined and clearly understood. It may then be possible to identify the means by which the difficulties can be overcome. The rational design of the prodrug can thus be divided into three basic steps: (1) identification of the drug delivery problem; (2) identification of the physicochemical properties required for optimal delivery; and (3) selection of a prodrug derivative that has the proper physicochemical properties and that will be cleaved in the desired biological compartment.

The difficulty of extrapolating data from animal to humans encountered during toxicokinetic and toxicologic studies with drugs is amplified with prodrugs, since not only metabolism of the active moiety might differ, but also its availability from the prodrug. As a matter of fact, there is presently no published rational for the conduct of animal and human pharmacokinetic programs during prodrug research and development.

- (f) *Amount of direction provided by the inventor* - the application is negligent regarding direction with respect to making and using substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein condition A is relevant, or pharmaceutically acceptable N-oxides, prodrugs, metabolites, amides or solvates thereof;
- (g) *Existence of working examples* - applicant has provided sufficient guidance to make and use substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein $R^1 = -H$ or $-C_{1-4}\text{alkyl}$; $R^2 = -H$ or $-C_{1-4}\text{alkyl}$; $X_1 = -H$ or $-C_{1-4}\text{alkyl}$; $X_2 = -H$ or $-C_{1-4}\text{alkyl}$; $X_3 = -H$ or $-C_{1-4}\text{alkyl}$; $X_4 = -H$ or $-C_{1-4}\text{alkyl}$; and $G_4 = -$

aryl, -heteroaryl or -cycloalkyl; however, the disclosure is insufficient to allow extrapolation of the limited examples to enable the scope of the tens of thousands of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, or pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates thereof. The specification lacks working examples of substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, or pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates thereof.

Within the specification, “specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula.” See MPEP § 608.01(p).

(h) *Quantity of experimentation needed to make or use the invention based on the content of the disclosure* - predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation (Jordan, V. C. *Nature Reviews: Drug Discovery*, 2, 2003, pp. 205-213).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. {*In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)}.

The determination that *undue experimentation* would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. (*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404). These factual considerations are discussed comprehensively in MPEP § 2164.08 (scope or breadth of the claims), § 2164.05(a) (nature of the invention and state of the prior art), § 2164.05(b) (level of one of ordinary skill), § 2164.03 (level of predictability in the

art and amount of direction provided by the inventor), § 2164.02 (the existence of working examples) and § 2164.06 (quantity of experimentation needed to make or use the invention based on the content of the disclosure).

Based on a preponderance of the evidence presented herein, the conclusion that applicant is insufficiently enabled for making and using sulfonamides and pharmaceutical compositions of the formula (I), wherein *condition A* is relevant, or pharmaceutically acceptable *N*-oxides, prodrugs, metabolites, amides or solvates of any substituted sulfonamides and pharmaceutical compositions of the formula (I), is clearly justified.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 132 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 132 recites the limitation *a compound according to claim 127 in line 1 of the claim*. There is insufficient antecedent basis, in claim 127, for this limitation, since claim 127 has been cancelled.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art

Art Unit: 4161

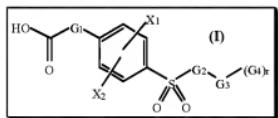
are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

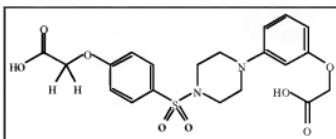
Claims 123-126, 130-133, 143 and 145 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Komoto, et al. in WO 93/012086, in view of Patani, et al. in *Chem. Rev.*, 96, 1996, pp. 3147-3176.

The instant application recites substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), shown to the left, where $G_1 = -C(R^1R^2)_nO-$, wherein $R^1 = -CH_3$



(C₁₋₄alkyl), $R^2 = -CH_3$ (C₁₋₄alkyl) and $n = 1$; $X^1 = -CH_3$ (C₁₋₄alkyl); $X^2 = -H$; $G_2 =$ -piperazine; $G_3 =$ -a single bond; and $G_4 =$ -Ph (aryl), which may be optionally substituted ($r = 1$ or 2), as modulators of peroxisome proliferator activated receptors (PPARs).

Komoto, et al. (WO 93/012086) teaches substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), shown to the right below, where $G_1 = -C(R^1R^2)_nO-$, wherein $R^1 = -H$, $R^2 = -H$ and $n = 1$; $X^1 = -H$; $X^2 = -H$; $G_2 =$ -piperazine; $G_3 =$ -a single bond; and $G_4 =$ -Ph (aryl), optionally substituted with $-OCH_2CO_2H$ (alkoxy), where $r = 1$, and hereafter referred to as 2-(4-(4-(3-



(carboxymethoxy)phenyl)piperazin-1-ylsulfonyl)phenoxy)acetic acid, as thromboxane receptor

antagonists, anticoagulants and anticholesteremics [p. 51, example 18].

Patani, et al. (*Chem. Rev.*, 96, 1996) teaches the relationship between -CH₃ groups and -H atoms as monovalent bioisosteres, which exert similar biological activity [p. 3148; column 1], via a direct adaptation of Grimm's Hydride Displacement Law [p. 3152, section A4; p. 3153 - column 1, ¶ 2; p. 3163, Table 12 - column 2].

The differences between the applicant's instantly recited substituted benzene sulfonamides and pharmaceutical compositions of the formula (I) and Komoto's substituted benzene sulfonamides and pharmaceutical compositions of the formula (I) are: a) R¹ = R² = -CH₃ (C₁₋₄alkyl) in the instantly recited substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), whereas R¹ = R² = -H in Komoto's substituted benzene sulfonamides and pharmaceutical compositions of the formula (I); and b) X¹ = -CH₃ (C₁₋₄alkyl) in the instantly recited substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), whereas X¹ = -H in Komoto's substituted benzene sulfonamides and pharmaceutical compositions of the formula (I).

The courts have recognized that *when expectation of similar properties stands unrebutted, it necessarily follows that expectation of similar uses also stands unrebutted, [with] expectation of similar use necessarily implying expectation of substantially equivalent substitute(s). Furthermore, there is no logical basis for distinguishing patentably between a prior art compound and a claimed novel compound *prima facie* obvious therefrom, even where a previously unknown or unobvious use has been found, where that use nevertheless inheres in both compounds and it is the compound *per se* that is claimed. {See *In re Hoch*, 57 CCPA 1292, 428 F.2d 1341, 166 USPQ 406 (1970)}.*

Consequently, since: a) Komoto teaches substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), wherein $R^1 = R^2 = X^1 = -H$, as thromboxane receptor antagonists, anticoagulants and anticholesteremics; b) Patani teaches $-CH_3$ groups and $-H$ atoms as monovalent bioisosteres, which exert similar biological activity; and c) the courts have recognized that when compounds are *prima facie* obvious, similar properties are directly related to similar uses of the compounds, one having ordinary skill in the art, at the time this invention was made, would have been motivated to combine the teachings of both Komoto and Patani and replace the hydrogens at R^1 , R^2 and X^1 in Komoto's substituted benzene sulfonamides and pharmaceutical compositions of the formula (I), with a $-CH_3$ group, with a reasonable expectation of success and similar therapeutic activity and utility, rendering claims 123-126, 130-133, 143 and 145 obvious.

Allowable Subject Matter

Claim 144 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DOUGLAS M. WILLIS, whose telephone number is 571-270-5757. The examiner can normally be reached on Monday thru Thursday from 8:00-6:00 EST. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan, can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. M. W./
Examiner, Art Unit 4161

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4161